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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,445	11/13/2001	A. Neil Barclay	DX 01052K1	1467

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DNAX RESEARCH INC.
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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/009,445	BARCLAY ET AL.	
	Examiner	Art Unit	
	Celine X. Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 9-24 are pending in the application.

This Office Action is in response to the Amendment filed on 11/13/06.

Response to Amendment

The rejection of claims 9-23 under 35 U.S.C. 112 2nd paragraph has been withdrawn in light of Applicant's amendment.

Claims 9-24 stand rejected under 35 U.S.C.101/112 1st paragraph for reasons set forth of the previous mailed on 7/13/06 and further discussed below.

Response to Arguments

In response to the utility rejection, Applicants argue that the office is requiring proof beyond a reasonable doubt regarding the precise mechanism of action of the CD200R protein in a specific cell and/or a particular disease, which is not the correct legal standard for utility. Applicants argue that the specification provides specific ands substantial utility for antibodies that bind to CD200R on page 74, lines 28-35, and page 75, lines 22-26, which discloses the therapeutic value of said antibody to diseases such as autoimmunity, inflammatory condition, tissue specific autoimmunity, etc., and in case of leukocytes, including macrophage/myeloid lineage cells, expressing the OX2R are involved in pathologies and contribute to disease process, the cell inhibitory activity of the receptor are mobilized. Applicants assert that such teaching provides substantial and specific utility for the claimed antibody. Applicants further cited Hoek et al. to demonstrate that CD200-/- mice have increased numbers of activated macrophages and a profound increase in susceptibility to autoimmune disease affecting brain and joint. Applicants also cite Gorczynki et al. to show the ability of CD200Fc to ameliorate collagen-induced arthritis

in mice, and anti-CD200R antibody elicits immunosuppression which permitting increased allograft survival in mice. Furthermore, Applicants cite Foster-Cuevas et al. to show that signaling through human CD200R down-regulates macrophage activation in the manner predicted by the multitude of murine and rat studies involving CD200/CD200R interactions. Applicants also point to Cherwinski et al. (WO 03/077947) to demonstrate the inhibitory effect of an antibody against human CD200R in a leukocyte population. Applicants further cite Cherwinski et al. (2005) to demonstrate that antibodies specific for human CD200R inhibited degranulation of human mast cells. Applicants assert that the collective information of the above references demonstrate that CD200R can act as an inhibitory signal in macrophages and mast cells, confirming the asserted utility of the specification. Applicants also argue that the teaching of Wright does not contradict the teaching of the specification in which an agonist antibody can modulate diseases disclosed in the specification. Finally, Applicants submitted *Ex parte* Hedrick in which the board determines that the antibody binds to the cytokine of IL-1 family has patentable utility, and assert that the instant application is similar to that case, thus the claimed antibody have patentable utility.

These arguments have been fully considered but deemed unpersuasive. Contrary to Applicant's assertion, the basis for the instant rejection is the specification lack teaching of a substantial, specific utility for the claimed invention at the time of filing. As discussed in the previous actions, the disclosure on page 74 and 75 of the specification is a laundry list of disorders that macrophages are involved in (ranging from stroke, neurodegeneration to autoimmune disorder such as multiple sclerosis), not disorders the polypeptide encoded by SEQ ID NO:20 is involved in. Although the rat OXRH1.2 (encoded by SEQ ID NO:2) is expressed

mainly on macrophages, it does not necessary mean that this receptor is involved in all types of disorder involving macrophages. Moreover, the specification does not teach whether the polypeptide encoded by SEQ ID NO:20, a homolog of the rat OXRH1.2, has the same expression pattern as the rat protein. In fact, the specification indicates that homologs of OXRH1.2, including human and rodent protein OXRH2-4 may not be closely related functionally (see page 88, lines 25-33). As such, based solely on the disclosure the cited text on page 74 and 75, the specification does not provide sufficient teaching of a substantial and specific utility for the claimed invention. Furthermore, the specification teaches that the polypeptide encoded by SEQ ID NO:20 is identified by sequence homology with SEQ ID NO:2, wherein SEQ ID NO:2 is a rat polypeptide that binds to OX2 antigen. As discussed in the previous office action, sequence homology alone cannot accurately predict function of the protein. As such, it is unclear whether SEQ ID NO:20 would have the same function as the protein encoded by SEQ ID NO:2, or those disclosed in the cited references. With regard to Hoek et al., this reference teaches the association between CD200 antigen and autoimmune disease, rather than the specific receptor of CD200R. Even if the receptor is involved in autoimmune disease, it is unclear whether the polypeptide encoded by SEQ ID NO:20 is the specific receptor for CD200 ligand for reasons discussed above. Moreover, this reference does not teach the relationship between the disease and the lack of the expression of CD200 is mediated through this specific CD200R encoded by SEQ ID NO:20. It is well known in the art many peptides may exert different effects through different pathways which is mediated through different receptors. There is no evidence suggest that this CD200R encoded by SEQ ID NO:20 is the only receptor which is responsible for the effect observed in the knockout mouse model as

disclosed in Hoek et al. With regard to Gorczynki et al., the disclosure of the ability of CD200Fc to ameliorate collagen-induced arthritis in mice and anti-CD200R elicits immunosuppression does not provide any information with regard to the utility of the polypeptide encoded by SEQ ID NO:20. Similarly, Foster-Cuevas et al. teach human herpes virus 8 K14 protein mimics CD200 in down-regulating macrophage activation through CD200 receptor, and both Cherwinski et al. teach the inhibitory signaling in mast cells through CD200 receptor. However, it is not clear from the record whether this CD200 receptor is the polypeptide encoded by SEQ ID NO:20. Most importantly, all the references cited above are post-filing art, in which the disclosure is not taught in the application, which cannot be used to substantiate a credible, substantial and specific utility of the claimed invention. The statue requires such utility to be taught in the application at the time of filing. In the instant case, a laundry list of the possible function does not constitute credible, substantial and specific utility for the claimed invention. The examiner acknowledges that an agonist of CDR200 may potentially modulate some of the diseases listed in the instant specification based on the teaching of Wright, however, the instant claims are not directed to an agonist of CDR200, rather, they are directed to an OX2R binding antibody or an antigen binding fragment. Moreover, the teaching of Wright is also post filing, which cannot be relied on to provide utility to the claimed invention at the time of filing.

Applicant's argument alleging examiner is requiring certain and exact data on biological role or function as did in the case of *Ex parte* Hedrick is not persuasive. The instant case differs from the *Ex parte* Hedrick because the IL-1δ belongs to IL 1 family, which is a well characterized cytokine family in which all of its member plays in a role of in systemic inflammatory reactions, whereas the instant polypeptide encoded by SEQ ID NO:20 is a

homolog of CD200R family member, which the function is not well defined at the time of filing. The instant specification states "isolation of the material bind to OX102 molecule and the N-terminal sequencing showed the putative CD200R is a novel molecule...preliminary analysis of the molecule does not reveal obvious motifs consistent with known signaling molecules although this does not exclude the potential role of this molecule in mediating OX2 delivered signals." Since this protein does not belong to a known receptor family of which all members are involved in a known function, clearly further research is required in determining the biological function of this putative OX2 receptor. MPEP set forth for the guideline in determining substantial utility "[A]n application must show that an invention is useful to the public as disclosed in its current form, not that it may prove useful at some future date after further research. Simply put, to satisfy the substantial utility requirement, an asserted use must show that the claimed invention has a significant and presently available benefit to the public." Fisher, 421 F.3d at 1371, 76 USPQ2d at 1230. Consequently, as discussed in the previous action, since the polypeptide encoded by SEQ ID NO:20 lacks utility at the time of filing, the binding compound to said polypeptide also lack utility. Therefore, this rejection is maintained.

In response to the enablement rejection, Applicants argue that the instant specification provides reasonable enablement for claimed antibodies and fragments thereof, including methods of making and guidance regarding kits containing the claimed antibody. Applicants argue that that the specification provides guidance for therapeutic use of antibodies at page 74 to 79, thus one skilled in the art would be able to make and use the claimed antibody. Applicants argue that there is no basis for evaluating the antibody based on method of treating disease and the antibody may be used in a diagnostic kit.

The above arguments have been fully considered but deemed unpersuasive. The reasons for the non-enablement of the claimed invention is set forth in the previous office action. The 112 1st statue requires the specification to teach how to make and use the claimed invention according to the embodiments disclosed in the instant specification. If treating diseases is the embodiment of the instant specification, it is required for the specification to provide sufficient teaching so one of skilled in the art would know how to use the claimed antibody to treat a disease. Merely stating the antibody can treat a disease without any supporting evidence is not sufficient teaching. With regard to the use of the antibody in a diagnostic kit, the disclosure of page 71-74 is directed to use of the antibody to identify the expression of a polypeptide. Since the specification does not teach a substantial and specific use for the polypeptide encoded by SEQ ID NO:20, the antibody to said polypeptide does not have a substantial and specific use either (see reasons set forth above). Therefore, this rejection is maintained.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X. Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELINE QIAN, PH.D.
PRIMARY EXAMINER